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Beyond appearance: Original vs Generic anticoagulants cost-benefit analysis

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Introduction

According to the WHO, generic drugs must satisfy quality requirements throughout the value chain. However, in the Peruvian case, this is not guaranteed.

Although the Peruvian regulatory framework requires compliance with good manufacturing, supply and distribution practices, therapeutic equivalence studies are not required for all generics. This is the case of Rivaroxaban, so that, at the date of this study, there is no guarantee that the generic has the same therapeutic effect as the innovative therapy (Rivaroxaban, Xarelto®).

In addition, even in countries where therapeutic equivalence is required, clinical studies have found that the original anticoagulants generate lower rates of thromboembolic events and deaths compared to generic drugs. In other words, they are more effective, so this is even stronger in countries where bioavailability error margins are lower..

Also, pharmacovigilance is a barrier to contain the margin of error in therapeutic equivalence studies. However, in the Peruvian case, even the health authority has stated that this policy still presents opportunities for improvement.

Therefore, the present study approximates and compares in monetary terms the costs and benefits associated with innovative therapy and those of its potential generics for patients with atrial fibrillation (AF) and deep vein thrombosis (DVT).

Objective

To perform a cost-benefit analysis within the Peruvian context to evaluate to what extent the innovative therapy (Rivaroxaban, Xarelto®), would be a better option compared to generic anticoagulants for a patient with atrial fibrillation (AF) or deep vein thrombosis (DVT).

Cost estimation method

Comparative analysis of costs and benefits of treatment with innovative therapy and its generic in the public and private sector. We addressed it through three stages:

1

Direct costs

Monetary quantification of the costs (treatment value) for 14 and 9 months for AF and DVT patients, respectively.

2

Indirect costs

Monetary quantification of the benefits (loss of lower productivity due to greater effectiveness of a treatment). A limitation for benefits quantification was that, up to the date of this study, there were no clinical evidence of Rivaroxaban generics effectiveness; therefore, we performed a systematic review of literature on the differences in effectiveness between innovative anticoagulants and their generics. Certain recent clinical studies found that the original anticoagulants (Warfarin and Enoxaparin) generate lower rates of occurrence of thromboembolic events and deaths compared to generic drugs, that is, they are more effective even in countries with an interchangeability policy implemented. It was selected the occurrence rates of warfarin in the USA because the interchangeability policy thresholds are the same as in Peru.

3

Weight

Estimation and comparison of the net benefit of the alternatives evaluated.

Results

We developed a systematic review of the literature, finding one paper that aimed to summaries best-evidence regarding the effectiveness and safety of generic versus brand-name drugs used in cardiology. In this review, two studies evaluated anticoagulants on the level of occurrence of thromboembolic events, hemorrhages and deaths: Helfritzsch et al. 2016, in Denmark, and Desai et al. 2018, in the US, both comparing Coumadin® (original) and Warfarin (generic).

In Denmark the bioavailability error margins require greater rigor. The range of error allowed to approve a generic equivalent is between [-10%, +11%]; while in the US between [-20%, +25%], both with a 90% confidence interval.

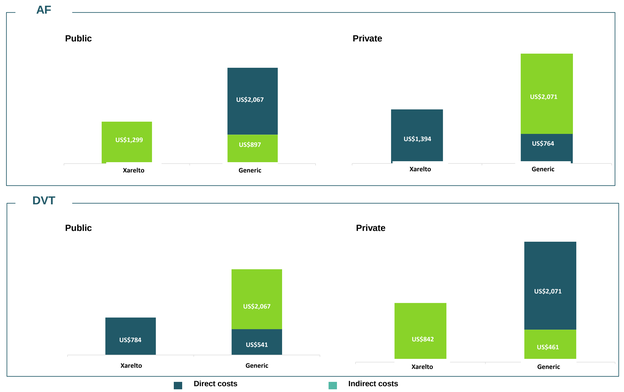
Additional cases per 10,000 patients used GENERIC drug

Country	Thromboembolic events	Deaths
Denmark	14	2
United State (US)	56	307

Note: Studies evaluate Warfarin.

Source: Hellfritzsch et al. 2016; Desai et al. 2018

Figure 1. Weighting of direct and indirect costs per patient in AF and DVT



Note: Exchange rate 2019: 3.34 PEN/USD (BCRP)

Extrapolated the differences in the rates of occurrence of thromboembolic events and deaths in the case of Coumadin (brand) and Warfarin (generic), assuming the estimated assumptions of the USA and considering cost data from Peru, innovative treatment has an incremental cost for AF of US$630 and US$403 compared to generic treatment in the private and public sector, respectively.

However, using considering the benefits, in monetary value, of the loss of productivity, and given our assumptions, we estimated that treatment with innovative therapy would save US$2,071 and US$2,067 in comparison of the treatment with a Rivaroxaban generic in the private and public sector, respectively. In the case of DVT, the results are similar for the private and public sector.

Although, these results do not consider the fact that Peruvian policy for generic drugs is incomplete in comparison to the one in the US, the literature is in consensus that the use of innovative drug has more benefits than the treatment with generics.

Conclusions:

The price of treatment with the generic could be lower than innovative therapy however, if the indirect costs due to lost productivity are considered, innovative therapy(Rivaroxaban, Xarelto®) becomes a less expensive alternative. Indeed, assuming the difference in effectiveness “innovative versus generic" of US Warfarin, it is obtained that the generic rivaroxaban is 2 times more expensive than the innovative therapy, both from the public and private perspective, for AF and DVT disease.

Given the limitation of the lack of data on the difference in effectiveness of generic rivaroxaban and innovative therapy, it is recommended to expand studies in the future and reduce the uncertainty of the present study.

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